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Breast Cancer Risk Assessment in 64,659 Women at a Single High-Volume Mammography Clinic

John T. Brinton, MS[1,*], **Lora D. Barke, DO**[2], **Mary E. Freivogel, MS CGC**[2], **Stacy Jackson, RT(R)(M)**[2], **Colin I. O'Donnell, MS**[1], and **Deborah H. Glueck, PhD**[1]

Lora D. Barke: Lora.Barke@riaco.com; Mary E. Freivogel: mary.freivogel@riaco.com; Stacy Jackson: Stacy.Jackson@riaco.com; Colin I. O'Donnell: Colin.ODonnell@ucdenver.edu; Deborah H. Glueck: Deborah.Glueck@ucdenver.edu

[1]Department of Biostatistics and Informatics, Colorado School of Public Health, University of Colorado Denver, 13001 E. 17th Place, Room W3125, Aurora, CO, USA, Office: 303-724-4358, Fax: 303-724-4489

[2]Invision Sally Jobe Breast Centers and Radiology Imaging Associates (RIA), 10700 E Geddes, Suite 200, Englewood, CO 80112, USA

Keywords

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Introduction

Breast cancer is the second leading cause of cancer deaths for women in the United States [1]. Despite recent controversy over screening regimens [2], several meta-analyses of randomized controlled trials demonstrate that mammography reduces mortality [3–5]. Presumably, screening reduces mortality by finding potentially fatal cancers early enough so that treatment is successful. In 2003, a total of 51,479,694 women (68% of the 73,858,958 women in the United States) reported using mammography in the past two years [6].

The sensitivity of digital mammography is about 70% [7]. Contrast enhanced magnetic resonance imaging (MRI) of the breast has a sensitivity of 88.1% [8]. In 2007, the American Cancer Society (ACS) issued guidelines suggesting that women at elevated risk for breast cancer be screened with breast MRI as an adjunct to mammography [9]. The ACS recommended screening with breast MRI and mammography in women 1) who have a *BRCA1/2* mutation, or are the untested first degree relative of a *BRCA1/2* mutation carrier; 2) who have a lifetime risk of breast cancer of 20% to 25% or greater, as defined by a risk model that takes into account extended family history; 3) who are at elevated risk because of an inherited cancer syndrome; or 4) who have had previous radiation therapy to the chest between 10 and 30 years of age.

*Corresponding author. john.brinton@ucdenver.edu.

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In this study, we collected the de-identified screening records of all 64,659 women presenting for breast cancer screening between January 2008 and January 2009 at Invision Sally Jobe Breast Centers, a private practice in the Denver metropolitan area. As the standard of care at Invision Sally Jobe, every woman presenting for screening mammography underwent risk assessment. If the women had 20% or higher lifetime risk of breast cancer, the radiologist reading the screening exam included in the mammography report a recommendation to the primary care physician that the woman receive breast MRI screening.

The results presented in this paper are from an observational study of a clinical implementation of the ACS recommendations at a single center, in single city. Thus, results may not be generalizable to other clinics. The risk assessment method and the process for recommending breast MRI screening in this study may not be the optimal way to implement the ACS recommendations. However, this is the first published report of any implementation of the ACS guidelines for breast MRI screening.

The purpose of this study is to estimate the proportion of women presenting for screening mammography who have a 20% or greater lifetime risk of breast cancer as determined by the Gail model [10,11]. As a second, exploratory aim designed to provide preliminary information for a proposed follow-up study, we report on the proportion of women who completed the recommended MRI at the same clinic which had conducted the risk assessment.

Materials and Methods

The study is an observational study, with a prospective cohort design. Women over 35 years of age presenting for mammography screening at Invision Sally Jobe between January 8, 2008 and January 7, 2009 were included in the cohort, for a total sample size of 64,659. For these women, de-identified data was excerpted from electronic medical records. The data included each woman's medical record number, age, date of birth, the date of screening, any history of cancer in relatives, the screening modality, the Breast Imaging Reporting and Data System category (BI-RADS®) [12], the recommendations from the radiologists and the Gail score. Both the HealthOne and the Colorado Multiple Institutional Review Board approved the study.

Invision Sally Jobe is a private practice with numerous clinical sites located throughout the Denver metropolitan area. They employ 17 breast radiologists who are board-certified and are either fellowship trained in breast imaging or have a minimum of ten years experience in breast imaging.

During the study period, Invision Sally Jobe used a two-step process to assess each patient’s lifetime risk of breast cancer. First, women presenting for routine screening mammography were asked if they had a first-degree maternal relative with breast cancer. Second, all women who reported a first-degree maternal relative with breast cancer were queried by the technologist to obtain the inputs for the Gail model. Inputs for the Gail model included previous history of biopsy (including history of either ductal carcinoma in situ or lobular carcinoma in situ), age, age at menarche, age at first live birth, number of female relatives with breast cancer (including mother, daughters, and sisters), number of previous breast biopsies, prior diagnosis with atypical hyperplasia, and race. In this study, race was input as Caucasian unless the woman was African American. The Gail model was used because the Gail model calculator posted on the National Cancer Institute website was readily accessible and easy to implement clinically in a high-volume mammography setting [13]. No other risk assessment models were used at the time of the study.

If a woman had a lifetime risk of 20% or greater, the radiologist recommended that the primary care physician issue an order for breast MRI screening, according to the ACS guidelines. The recommendation was included in the mammography report. Women were not personally notified of their lifetime risk or the recommendation for breast MRI screening.

A breast MRI exam was considered to be a screening exam if it occurred after any examination which had been given a BI-RADS score of 1, 2, or 3. A breast MRI exam was considered to be a diagnostic exam if it occurred after any examination which had been given a BI-RADS score of 0, 4, or 5 or if the patient was symptomatic. A breast MRI exam which occurred at the same visit as a screening mammogram was considered to be a screening breast MRI exam regardless of whatever score the mammogram eventually received.

Two-view screening mammography was performed on either a Hologic Selenia® (Hologic Inc., Bedford, MA) or Fischer SenoScan® (Fisher Medical Imaging, Broomfield, CO) full-field digital mammography unit. Softcopy images were interpreted on a Sectra (Sectra Medical Systems, Linköping, Sweden) digital mammography workstation. Breast MRI screening was performed on a GE (GE Healthcare, Waukesha, WI) Signa® LX 1.5T scanner using an 8-channel breast coil. The clinical protocol consists of axial 4mm thick contiguous fat-suppressed T2-weighted STIR imaging, followed by axial 1.6 – 2.0mm thick overlapped T1 volumetric VIBRANT™ fat-suppressed imaging through both breasts. Dynamic scanning included imaging that was performed before and serially after the intravenous power injection of a weight-based dose (ranging from 13-20 ml) of gadopentetate dimeglumine, Magnevist® (Bayer HealthCare© LLC, Pharmaceutical Division, Wayne, NJ) gadolinium contrast. Post-contrast images were performed every 3 minutes for 9 minutes total. Interpretation was carried out on picture archiving and communication systems (PACS) workstations using CADstream MRI CAD software (CADstream®, Merge Healthcare, Milwaukee, WI) for image subtraction, multiplanar reformatting and kinetic analysis. Additional evaluation of MRI findings was performed primarily with ultrasound (Logiq 9, GE Medical Systems). MR-guided vacuum-assisted biopsy is available and was performed as needed using the SenoRx (SenoRx Inc., Irvine, CA) vacuum-assisted MRI biopsy device and an 8-channel biopsy coil.

Statistical Analysis

Fisher's exact test was used to assess association in two-by-two tables. The Fisher's exact test is an appropriate test when neither of the margins for the tables are determined in advance [14]. All tests for the were two-sided tests using an alpha level of 0.05.

Results

Summaries of the study population stratified by age and risk are given in Tables 1 and 2. The mean age of all women presenting for mammography screening was 55 (range 35–97) years old. 1,772 (3%) were younger than 40 years. 21,407 (33%) were between 40 and 50 years old. 41,480 (64%) were 50 years or older. 53,871 (83%) women reported no first-degree relative with breast cancer and had no recorded Gail score. Technologists evaluated 10,788 (17%) of the total women using the Gail model.

For the 10,788 women with a recorded Gail score, the average score was 14.3% (range 0.4%–52.0%). Women younger that 40 had an average Gail score of 18.3% (range 0.6%–45.5%). Women 40 or older had an average Gail score of 14.2% (range 0.4%–52.0%). On average, women who were younger that 40 had Gail scores significantly higher than women who were older than 40 ($t = 15.8$, $p < 0.0001$). 1,246 (11.5% of 10,788) women had a

lifetime risk of breast cancer of 20% or greater, and 436 (4% of 10,788) women had a lifetime risk of breast cancer 25% or greater.

Columns 2 and 3 of Table 2 show the number of women in each age group for whom the radiologist issued a recommendation for breast MRI screening. Of the 1,772 women younger than 40 years, the radiologist issued a recommendation for breast MRI for 97 (5.5%). Of the 62,887 women 40 years and older, the radiologist issued a recommendation for breast MRI for 1,149 (1.8%). The radiologist was 3.1 times more likely to issue a recommendation for breast MRI for women under 40 than for women 40 and over (95% CI: 2.5 to 3.8, Fisher's exact $p<0.0001$).

Overall, radiologists issued recommendations for breast MRI in addition to mammography for 1,246 (1.9% of 64,659) women. Of those women, 173 (13.9%) had a screening breast MRI within one year of the recommendation at the same clinic where the initial screening and risk assessment took place. Column 4 of Table 2 shows the women stratified by age group. There was no significant difference in completion rate at the recommending clinic between women younger than 40 and women 40 and over (OR 1.4 95% CI: 0.78 to 2.3, Fisher's exact $p<0.28$).

Of the 173 women who completed the breast MRI screening at the recommending clinic, 109 (54%) did so within the first two months after the recommendation was made. By six months after the recommendation, 108 women (71%) had completed breast MRI screening at the clinic. The median time to completion of breast MRI screening at the recommending clinic was 65 days with first and third quartiles at 27 days and 182 days respectively. The longest time to completion of breast MRI screening at the recommending clinic was one year. The mean time to completion of breast MRI screening at the clinic was 114 days.

Discussion

Although previous literature has explored breast cancer risk assessment and identification of women at elevated risk, it has not examined the clinical implementation of the ACS recommendations for breast MRI screening in high risk women (Saslow *et al.*, 2007). Murphy *et al.* (2008) conducted risk assessment in 18,190 women over two years at the Avon Comprehensive Breast Evaluation Center to identify candidates for screening MRI. Murphy *et al.* (2008) found 78 (0.43%) of the women had ≥ 20% lifetime risk of breast cancer as determined by the BRCAPRO risk model. Berg *et al.* (2010) described MRI screening in the context of an ACRIN trial of high risk women. Even in the context of their clinical trial, 42.1% of the women declined MRI screening.

Although recommendations for the use of MRI as an adjunct to mammography were made by the ACS in 2007 (Saslow et al., 2007), we could find no papers that described a clinical risk assessment process which led to MRI screening for high risk women. This paper describes how risk assessment was implemented in a single high-volume mammography clinic and details the proportion of women who were found to be of high risk. We also describe the number of women at high risk who returned to the recommending clinic for MRI screening.

Limitations of the Study and of the Clinical Protocol for Risk Assessment

The study described in this was conducted as single clinic, unfunded pilot study designed to obtain preliminary data for a planned trial. Thus, it had several limitations. The study was an observational study based on de-identified electronic medical records. We could not determine what recommendations women received from their primary care physician, what they understood, and how they made decisions about whether to pursue additional screening.

We also could not determine how the primary care physicians felt about the ACS recommendations or what they recommended to their patients. In addition, the study probably under-estimated the number of women found to be high risk who eventually obtained an MRI. We were unable to track women who sought further screening and care at other clinics. Some women may have completed their breast MRI screening elsewhere.

The clinical protocol described in the study was an initial implementation of the ACS recommendations for breast MRI screening. Reviewing the results of the study with the clinical co-authors has resulted in several improvements in their current clinical protocol.

1. All women screened in Invision Sally Jobe now receive model-based risk assessment. During the study period, only women with a first-degree maternal relative with breast cancer were assessed using a model.
2. Invision Sally Jobe will soon implement the use of the Tyrer-Cuzick model for risk assessment (Tyrer et al., 2004) for all patients. The Tyrer-Cuzick model accounts for a history of cancer in second-degree relatives. During the study period, the clinic used the Gail model because of its accessibility and ease of use in practice. However, Saslow *et al.* (2007) "do not recommend [the Gail model's] use for evaluating patients for breast MRI screening." Saslow *et al.* (2007) instead suggest using the BRCAPRO, Tyrer-Cuzick, or Claus models [16–20].
3. Invision Sally Jobe now communicate recommendations directly to women who are at 20% or higher lifetime risk of breast cancer, in addition to their primary care physicians. A personalized letter is sent directly to the woman. The woman's primary care physician receives a copy of the letter and the imaging report. The letter suggests that the woman consider breast MRI screening and discuss breast MRI screening with her primary care physician.

During the study period, the primary care physician received the recommendation on the mammography report. No letter was sent directly to the woman. Thus, if the primary care physician did not communicate the recommendation for breast MRI screening, some women may have been unaware of the recommendation for breast MRI screening.

Future studies

While the current study had limitations in both the study design and the clinical protocol, it raises many important questions for future research. Only by asking women and physicians directly can we hope to understand the reasons they comply with the ACS recommendations or make informed decisions not to comply. In addition, we must understand how financial issues influence decisions about care by talking to women about out-of-pocket costs and evaluating reimbursement information from insurance providers.

The clinical protocol followed at Invision Sally Jobe during the study period has now changed in many ways. In an effort to improve care, the clinic changed the model used to assess risk, and the way the recommendation is made to women and their primary care physicians. We plan to study outcomes under the new and improved clinical protocol.

It is important to study the clinical effectiveness of the ACS guidelines, as well as examine barriers to implementation of the guidelines. Additional screening can cause both benefits and harms. Examining the stage and grade of MRI-detected cancers, and comparing them to the stage and grade of mammography-detected cancers would provide an early indication of utility. We hope to tabulate harms, including additional recalls and biopsies, and to talk to women about any anxiety and pain resulting from the adjunct breast MRI screening and any exams resulting from the adjunct screening exam.

Conclusion

Our study provides important information about the proportion of women at elevated risk for breast cancer at a single high-volume mammography clinic. The information is relevant to clinicians interested in implementing risk assessment at their own clinic. Our study also raises many important, unanswered questions about the best method of implementing adjunct breast MRI screening for women with an elevated lifetime risk of breast cancer.

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Table 1

Study population cross classified by lifetime risk for breast cancer and reported maternal family history

Gail lifetime risk	Family history	No family history*
<20%	9,612 (14.9)	53,871 (83.3)
20%–25%	745 (1.2)	-
>25%	431 (0.7)	-

Note- Data in parenthesis is the percent of the total N=64,659.

* Gail score not calculated, and assumed to be lower than 20%.

Table 2

Breast MRI screening recommendations and completion by age group

Age	Overall	MRI recommended		MRI completed	
		Yes	No	Yes	No
<40	1,772 (2.7)	97 (0.1)	1,675 (2.6)	17(1.4)	80 (6.4)
40–49	21,407 (33.1)	498 (0.8)	20,909 (32.4)	73 (5.9)	425 (34.1)
≥50	41,480 (64.2)	651 (1.0)	40,829 (63.2)	83 (6.7)	568 (46.6)
Total	64,659 (100.0)	1,246 (1.9)	63,413 (98.1)	173 (13.9)	1,073 (86.1)